K-04

Soluble Glycoprotein 120 is associated with Coronary Artery Inflammation Measured by Pericoronary Fat Attenuation Index.

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BACKGROUND

People living with HIV face an increased risk of cardiovascular. Viral antigens, such as the HIV-1 envelope subunit glycoprotein (gp120), have been shown to persist in plasma even when viral load is suppressed, and may directly contribute to vascular inflammation and CVD.

HYPOTHESIS

In people living with HIV, the presence of sgp120 in plasma leads to sustained inflammation, driving cardiovascular disease.

The pericoronary fat attenuation index (PFAI), which measures the computed tomography attenuation of pericoronary adipose tissue, has emerged as a robust, non-invasive biomarker that predicts overt cardiovascular disease, even after adjusting for CVD risk factors and coronary plaque characteristics. Higher values (closer to -30 HU) indicate more inflammation and increased CVD risk.



Figure - post-processing of cardiac computed tomography angiography images to obtain PFAI

The presence of HIV glycoprotein 120 in the plasma of aviremic people living with HIV is associated with increased inflammation in pericoronary fat.

METHODS

Participants were recruited from the Canadian HIV and Aging Cohort Study. Sgp120 was measured by an in-house ELISA (previously published.) We developed multivariable linear regression models to assess the adjusted association between sgp120 and PFAI.

PFAI MEASUREMENT

We obtained PFAI by calculating the mean attenuation of all fat voxels (defined as those with an attenuation between -190 and -30 Hounsfield units [HU]) located within a radial distance from the outer vessel wall equal to the vessel's diameter, in the segment of the right coronary artery situated 10 to 50 mm from the ostium.

Participants' characteristics (N=145)	
Percent male	90%
Mean age	56 years
Current smoking	29%
High blood pressure	31%
Diabetes	9%
Current statin treatment	21%
Detectable plaque on CCTA	65%
Detectable sgp120 in plasma	45%
Mean Current CD4	628
Nadir below 200	47%
Mean duration of HIV	19 years

Crude and adjusted associations between risk factors and pericoronary fat attenuation index

	Beta (95%CI)	P value	Beta (95% CI)	P value
Age	0.13 (-0.10 to 0.37)	0.26		
Female sex	-6.95 (-12.09 to -1.80)	0.009	not included due to small cells	
HIV duration	-0.06 (-0.26 to 0.14)	0.56		
Detectable soluble gp120	3.28 (0.20 to 6.36)	0.037	3.04 (0.004 to 6.09)	0.050
Statin treatment at CT	-3.58 (-7.38 to 0.22)	0.065	-3.69 (-7.41 to 0.02)	0.051
CD4:CD8 ratio	-2.14 (-5.52 to 1.24)	0.21		
Current smoking	3.59 (0.21 to 6.97)	0.038	3.30 (-0.03 to 6.64)	0.052
Diabetes	-0.51 (-5.89 to 4.88)	0.85		
High blood pressure	2.87 (-0.44 to 6.17)	0.089		
LDL	-1.12 (-2.78 to 0.55)	0.187		
HDL	-1.60 (-5.03 to 1.82)	0.36		

RESULTS

Presence of CVD on CCTA was associated with higher PFAI (-77 HU vs -81 HU, p=0.028). Soluble gp120 was detectable in 65 (45%) participants and was associated with higher PFAI (-77 HU vs -80 HU, *p*=0.037).

CONCLUSIONS

Our data support the hypothesis that sgp120, even during suppressive antiretroviral therapy, may contribute to cardiovascular disease in People living with HIV by increasing coronary inflammation. More data is needed to assess sex-differences and longitudinal values.

ADDITIONAL KEY INFORMATION

Residual viral products may represent a novel treatment target to reduce comorbidity in PWH. **The RESTART trial**, currently underway at our center, is testing whether adding fostemsavir to optimized background therapy for **people with undetectable HIV viral load but detectable sgp120** will lead to reduced systemic inflammation and cardiovascular disease.

PLAIN LANGUAGE SUMMARY

In people living with HIV, viral proteins can be detected in plasma even when viral load is undetectable, and they may contribute to comorbidities. In this experiment, we show that the presence of gp120 in plasma is associated with increased inflammation in the fat surrounding coronary arteries, a marker linked to an increased risk of heart disease.